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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,601	05/01/2001	Alfred S. Lewin	36689.140	7183

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
11/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/847,601	LEWIN ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,14-43,53,58 and 59* is/are pending in the application.

4a) Of the above claim(s) *43 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,14-42,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

The finality of the previous Office action mailed 03/14/2008 is withdrawn. Claims 1, 4, 14-43, 53, 58 and 59 are pending. Claims 1, 4, 8, 14-42, 58 and 59 are currently under examination. Claims 43 and 53 are withdrawn as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 14-42, 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wraight et al. (cited on PTO Form 892 mailed 09/27/2006), Thompson et al. (U.S. Patent No. 5,750,390), Pavco et al. (cited on PTO Form 892 mailed 09/27/2006), Kido et al. (cited on PTO Form 892 mailed 09/27/2006) and Tang et al. (US Patent No. 6,348,450).

The instant claims are drawn to a ribozyme that specifically cleaves an mRNA encoding a polypeptide that causes or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye (claim 1), wherein the ribozyme specifically cleaves an mRNA that comprises a nucleotide sequence having SEQ ID No.

88, wherein the ribozyme has a sequence of SEQ ID No. 100, wherein the ribozyme is a hammerhead or hairpin ribozyme (claims 14-15) and further drawn to a vector comprising a polynucleotide encoding said ribozyme and a promoter (claim 16). The instant claims are further drawn to a host cell, wherein said host cell is mammalian or a human cell (claims 30-32) and drawn to a composition, wherein said composition further comprises a pharmaceutical excipient (claims 36-37 and 39) and drawn to a kit wherein said kit comprises a composition (claims 40-41).

Wraight et al. teach an antisense oligonucleotide that binds to and inhibits expression of a sequence comprising SEQ ID NO. 88 (see IGF-I oligonucleotide #2501) and teach IGF-1 is involved in neovascularization of the retina (see page 21, lines 6-15). Wraight et al. does not teach the oligonucleotide is a ribozyme and further does not teach a vector comprising a promoter and a ribozyme, a host cell comprising a ribozyme, a composition or a kit comprising a ribozyme and does not teach a vector wherein said promoter element directs expression of said polynucleotide in a retinal cell, a photoreceptor cell, a rod or cone cell, a Mueller cell or wherein said promoter comprises a mammalian rod opsin promoter element.

Thompson et al. teach ribozyme molecules and teach the enzymatic nature of ribozymes is advantageous over technologies such as antisense technologies (see column 2). Thompson et al. teach the method steps of designing ribozymes to target any gene and teach selecting suitable target sites and synthesizing and testing said ribozymes for efficient cleavage (see columns 5-6). Thompson et al. further teach ribozymes can be hammerheads or hairpins (see column 13), teach expression vectors

comprising promoters that direct expression of the ribozymes, including constitutive promoters such as CMV (see column 8), teach ribozymes in mammalian host cells (see column 3) and teach pharmaceutical compositions comprising liposomes and ribozymes (see column 10).

Pavco et al. teach adeno-associated viral vectors for expression of ribozymes (see column 6) and teach the use of ribozyme as diagnostic reagents and further teach a delivery device, such as filter disks comprising a ribozyme and a solution suitable for delivery to the eye that is surgically implanted into a mammalian eye for delivery of said ribozyme composition (see columns 21-22 and Example 11).

Kido et al. teach use of a viral vector comprising a mouse opsin promoter to deliver therapeutic genes (see page 833 and Figure 1). Kido et al. teach said opsin promoter directs expression in photoreceptor cells, which comprise rod and cone cells, and directs expression in Mueller cells (see page 838 second column and Figure 8C).

Tang et al. teach kits for therapeutic and diagnostic use comprising oligonucleotides and pharmaceutically acceptable carriers wherein the composition is packaged and labeled in a container that contains instructions for administration of said composition (see column 8, lines 10-20).

It would have been obvious to one of skill in the art at the time of the instant invention to substitute a ribozyme for an antisense molecule, as taught by Thompson et al., to inhibit expression of a gene encoding IGF-I, a polypeptide involved in neovascularization of the retina, as taught by Wraight et al. It would have further been obvious to make any ribozyme sequence as taught by Thompson et al. that targets an

IGF-1 gene and deliver the ribozyme using filter disks as taught by Pavco et al. as well as package for therapeutic use and further obvious to use a mouse opsin promoter as taught by Kido et al.

At the time of the instant invention, it was well known in the art that ribozymes were more advantageous over antisense technologies because of the efficient cleavage and enzymatic properties: a single ribozyme molecule is able to cleave many molecules of a target RNA. One of ordinary skill in the art in looking to inhibit the expression of IFG-1 would have wanted to substitute the antisense compound taught by Wraight et al. with a ribozyme molecule as taught by Thompson et al. Thompson et al. teach ribozymes are advantageous over antisense oligonucleotides since the effective concentration of ribozymes necessary to effect therapeutic treatment is lower than that of antisense oligonucleotides (see col. 2). Moreover, given that Thompson et al. details the steps necessary to select a target site and design and test a ribozyme that is capable of efficiently cleaving a target, it would have been a matter of routine optimization for the skilled artisan to design a ribozyme having SEQ ID No. 100 that is capable of cleaving a mRNA encoding an IGF-1 receptor polypeptide.

One of ordinary skill in the art would have wanted to delivery the ribozyme using filter disks taught by Pavco et al. given Pavco et al. teach efficient ribozyme mediated inhibition in the eye of a subject when the ribozyme was delivered using said delivery method and in looking to inhibit IGF-1 expression in a cell or tissue of the eye, one would have used said delivery method. One of skill in the art would have clearly been motivated to incorporate a mammalian opsin promoter because Kido et al. teach a viral

vector comprising an opsin promoter is capable of selectively directing expression of therapeutic genes to photoreceptor cells (see page 841, last paragraph). One of skill in the art would want to make a vector comprising an opsin promoter to specifically express ribozymes targeted to VEGF in retinal cells for the purpose of decreasing expression of VEGF, which contributes to disease of the eye, such as retinopathy. Moreover, one would have been motivated to package the composition into a kit for diagnostic or therapeutic use.

Finally, one would have had a reasonable expectation of success at making a ribozyme targeted to IGF-I given that the IGF-I sequence was known, as evidenced by Wraight et al. who teach making specific inhibitory sequences targeted to IGF-I, and further given that Thompson et al. provides a detailed disclosure of how to make any ribozyme targeted to any sequence. One would have had a reasonable expectation of success given that Pavco et al. teach specific embodiments of administration ribozyme targeted to genes that cause or contributes to diseases or disorders of the eye using filter disks and given that Kido et al. teach an opsin promoter incorporated into a vector directs expression of a gene in retinal cells, specifically photoreceptors and Mueller cells.

Thus, in absence of evidence to the contrary, the invention would have been *prima facie* evident to one of ordinary skill in the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Examiner
Art Unit 1635